A Review: Transdermal Drug Delivery System

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Abstract- *Transdermal drug delivery has been recognised as a non-invasive drug delivery option. Transdermal systems are designed to deliver medications to the systemic circulation in a controlled and continuous manner through the skin. The usage of penetration enhancers, which improve the stratum corneum's permeability. Permeation enhancers are defined as substances that are capable of promoting penetration of drugs into skin and transdermal therapeutic systems offers a more reliable mean of administering drug through the skin. This article provides an overview on structure of skin and barrier, penetration enhancer, formulation and evaluation. Today about 74% of drugs are taken orally and are found not to be as effective as desired. To improve such characters transdermal drug delivery system has emerged. Drug delivery through the skin to achieve a systemic effect of a drug is commonly known as transdermal drug delivery and differs from traditional topical drug delivery. Transdermal drug delivery systems (TDDS) are dosage forms that involve drug transport to viable epidermal and or dermal tissues of the skin for local therapeutic effect while a very major fraction of drug is transported into the systemic blood circulation. However, the skin, in particular the stratum corneum, poses a formidable barrier to drug penetration thereby limiting topical and transdermal bioavailability. Skin penetration enhancement techniques have been developed to improve bioavailability and increase the range of drugs for which topical and transdermal delivery is a viable option. During the past decade, the number of drugs formulated in the patches has hardly increased, and there has been little change in the composition of the patch systems. It is intended to improve the therapeutic efficacy and safety, maintain the steady state plasma level of drugs and overcome the significant drawbacks of the conventional oral dosage forms and parenteral preparations. It is ideally suited for the diseases that demand chronic treatment with frequent dosing. This review deals with a brief insight on the introduction, the formulation aspects, the physical and chemical enhancers explored or being explored to enhance the transdermal delivery of drugs across the stratum corneum, the evaluation parameters (physicochemical, in vitro, in vivo studies) and therapeutic applications of TDDS.*

Keywords- Transdermal drug delivery system, Skin, Penetration enhancers.

I. INTRODUCTION

The transdermal drug delivery system (TDDS), commonly known as "patches," is a dosage form that is designed to distribute a therapeutically effective amount of drug over the skin of a patient. The overall morphological, biophysical, and physiochemical aspects of the skin must be studied in order to transfer medicinal agents via the human skin for systemic action.[52] Transdermal delivery not only allows for controlled, consistent drug administration, but it also allows for continuous input of medications with short biological half-lives and prevents pulsed entry into systemic circulation, which can result in undesirable side effects. Transdermal drug delivery systems, controlled release systems, transmucosal drug delivery systems, and so on are examples of novel drug delivery methods. Transdermal drug delivery systems (TDDS), also known as patches, are dosage forms designed to deliver a therapeutically effective amount of drug across a patient's skin. To deliver therapeutic agents through the human skin for systemic effects, the comprehensive morphological, biophysical, and physicochemical properties of the skin are to be considered. Transdermal delivery provides a leading edge over injectables and oral routes by increasing patient compliance and avoiding first-pass metabolism espectively1. Transdermal delivery not only provides controlled, constant administration of the drug, but also allows continuous input of drugs with short biological half-lives and eliminates pulsed entry into the systemic circulation, which often causes undesirable side effects. Thus various forms of Novel drug delivery systems such as Transdermal drug delivery systems, Controlled release systems, Transmucosal delivery systems, etc. emerged. Several important advantages of transdermal drug delivery are limitation of hepatic first-pass metabolism, enhancement of therapeutic efficiency, and maintenance of steady plasma level of the drug. The first Transdermal system, Transderm-SCOP was approved by FDA in 1979 for the prevention of nausea and vomiting associated with ravel, particularly by sea. With the introduction of the first transdermal patch of scopolamine in 1979, the transdermal drug delivery has made an important contribution to the medical practice in the past three decades but is yet to be recognized as a major alternative to the oral delivery and hypodermic injections (Langer, 2004; Prausnitz et al., 2008). The major obstacle for the topical drug delivery is the low diffusion rate of drugs across the relatively

impermeable, outermost skin layer, the stratum corneum (Bouwstra et al., 2002). Besides, the intercellular lipid region, the major pathway for lipophilic drugs, has a diffusion path length of about 500mm which is much longer than the thickness of stratum corneum (20 mm) (Gaur et al., 2009; Phillips et al., 1995). Tablets and injections have been the traditional way to take medications; new options are becoming increasingly popular.

II. SKIN STRUCTURE

With a surface area of 1.7 m2 , skin is the most accessible and largest organ of the body, accounting for 16 percent of an average person's total body mass.[1,2,3] The skin's primary role is to protect the body from germs, ultraviolet (UV) radiation, chemicals, allergies, and water loss by acting as a barrier between the body and the external environment.

The three main regions of the skin are :

1) Epidermis : The multilayered epidermis varies in thickness, depending on cell size and number of cell layers of epidermis, ranging from 0.8 mm on palms and soles down to 0.06 mm on the eyelids. Table 1 gives thickness, water permeability and diffusivity of water through epidermis. It consists outer stratum corneum and viable epidermis.

A) Stratum corneum : This is the outermost layer of skin also called as horney layer. It is approximately 10µm thick when dry but swells to several times this thickness when fully hydrated. It contains 10 to 25 layers of dead, keratinized cells called corneocytes. It is flexible but relatively impermeable. The stratum corneum is the principal barrier for penetration of drug. The architecture of horney layer may be modeled as a wall-like structure. In this model, the keratinized cells function as protein “bricks” embedded in lipid “mortar.” The lipids are arranged in multiple bilayers.

B) Viable epidermis : This is situated beneath the stratum corneum and varies in thickness from 0.06mm on the eyelids to 0.8mm on the palms. Going inwards, it consists of various layers as stratum lucidum, stratum granulosum, stratum spinosum and the stratum basal. In the basale layer, mitosis of the cells constantly renews the epidermis and this proliferation compensates the loss of dead horney cells from the skin surface. As the cells produced by the basal layer move outward, they alter morphologically and histochemically, undergoing keratinization to form the outermost layer of stratum corneum.

2) Dermis : Dermis is 3 to 5mm thick layer and is composed of a matrix of connective tissue, which contains blood vessels, lymph vessels and nerves. The cutaneous blood supply has essential function in regulation of body temperature. It also provides nutrients and oxygen to the skin while removing toxins and waste products. Capillaries reach to within 0.2 mm of skin surface and provide sink conditions for most molecules penetrating the skin barrier. The blood supply thus keeps the dermal concentration of a permeant very low and the resulting concentration difference across the epidermis provides the essential concentration gradient for transdermal permeation.

3) Hypodermis : The hypodermis or subcutaneous fat tissue supports the dermis and epidermis. It serves as a fat storage area. This layer helps to regulate temperature, provides nutritional support and mechanic al protection. It carries principal blood vessels and nerves to skin and may contain sensory pressure organs.

Barrier to drug permeation -

The stratum corneum The dead cells of the stratum corneum, which hinder the inward and outward circulation of drug substances and have a high electrical resistance, are the principal barriers to absorption. The stratum corneum is a heterogeneous tissue made up of keratinized cells that have been flattened. The outer layers of these cells are less densely packed than the granular layer beneath them. As a result, the epidermal barrier becomes more impermeable in the lower region, raising the possibility that a second barrier, the stratum corneum, exists at this level. These horny cells have no nuclei and are therefore physiologically inactive.

Penetration enhancers –

Permeation enhancers are defined as substances that are capable of promoting penetration of drugs into skin and transdermal therapeutic systems offers a more reliable mean of administering drug through the skin.

Advantages –

1. Using penetration enhancers, increase the drug's penetration rate to a level that is sufficient for therapeutic efficacy.
2. It is useful for facilitating the absorption of non-absorbable medicines through the skin.
3. It can promote transdermal absorption of topical preparation.

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Polymer used in transdermal drug delivery system –

The backbone of TDDS is polymers, which regulate the drug's release from the device. The drug can be dispersed in a liquid or solid state synthetic polymer basis to create a polymer matrix. Furthermore, they must distribute a medicine consistently and effectively throughout the product's stated shelf life and must be safe.

Adhesives –

All transdermal devices are attached to the skin with a pressure sensitive adhesive that can be placed on the device's face or in the rear and extends peripherally.

Rservoir system –

The drug reservoir is placed between an impermeable backing layer and a rate-controlling membrane in this system. The drug can be released through a rate-controlling membrane that is either microporous or nonporous. The drug can be in the form of a solution, suspension, gel, or dispersed in a solid polymer matrix in the drug reservoir compartment.

III. FACTORS AFFECTING TRANSDERMAL PERMEATION

1) Biological factor

Skin conditions: The intact skin itself acts as a barrier but many agents like acids, alkali cross the barrier cells and penetrates through the skin, many solvents open the complex dense structure of horny layer Solvents like methanol, chloroform remove lipid fraction, forming artificial shunts through which drug molecules can pass easily.

Skin age: It is seen that the skin of adults and young ones are more permeable than the older ones but there is no dramatic difference. Children show toxic effects because of the greater surface area per unit body weight. Thus, potent steroids, boric acid, hexachlorophene have produced severe side effects.

Blood Supply: Changes in peripheral circulation can affect transdermal absorption. Skin metabolism: Skin metabolizes steroids, hormones, chemical carcinogens and some drugs. So, skin metabolism determines the efficacy of drug permeated through the skin. Species differences: The skin thickness, density of appendages, and keratinization of skin vary from species to species, so affects the penetration.

2) Physicochemical factors:

Skin hydration: In contact with water the permeability of skin increases significantly. Hydration is most important factor in increasing the permeation of skin. So use of humectant is done in transdermal delivery.

Temperature and pH: The permeation of the drug increases ten folds with temperature variation. The diffusion coefficient decreases as the temperature falls

IV. APPLICATION OF TDDS

- The antihypertensive drug like clonidine and ketoprofen, the non-steroidal antiinflammatory drug are also available in the form of transdermal patches.
- Estrogen patches are sometimes prescribed to treat menopausal symptoms as well as postmenopausal osteoporosis.
- Other transdermal patches for hormone delivery include the contraceptive patch.
- Transdermal delivery agent for Attention Deficit Hyperactivity Disorder (ADHD).
- Two opioid medications used to provide round-the-clock relief for severe pain are often prescribed in patch form: Fentanyl and Buprenorphine.

V. CONCLUSION

TDDS has gained realistic potential as the next generation drug delivery system for the prolonged, controlled release of both hydrophobic and hydrophilic drugs, efficiently addressing the low oral bioavailability and inconvenience of injections. Future research will be aimed at better transdermal device design with greater understanding of the different mechanisms of biological interactions with permeation enhancers and improving the flux for a wide variety of molecules especially macromolecules and vaccines using cost effective, novel physical enhancement techniques along with the existing chemical enhancers. Less absorption, more uniform plasma levels, improved bioavailability, decreased adverse effects, efficacy, and product quality are all advantages of using a transdermal drug delivery system for therapeutic therapy. When it comes to providing medication to

small children and the elderly, transdermal distribution enhances and simplifies patient compliance. Penetration enhancers are used to increase the drug availability through intact skin. This article discusses the nature of the skin and its barrier, as well as penetration enhancers, formulation, and evaluation of transdermal patches. The transdermal medication delivery system has the potential to become one of the greatest innovative drug delivery systems in the future. Successful transdermal drug application requires numerous considerations. Bearing in mind that the basic functions of the skin are protection and containment, it would seem exceptionally difficult to target the skin for drug delivery. However, with our greater understanding of the structure and function of the skin, and how to alter these properties, more and more new drug products are being developed for transdermal delivery.

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